

a! which is a divisional application of USSN 07/979638 (now abandoned), filed November 20, 1992, which --.

In the specification at page 1, line 10, after "07/897,778," please insert --(now abandoned)--.

In the Claims

Cancel claims 9, 10, 11, 22, 25-27, 33, 35, and 40.

Amend claims 1-4, 8, 12-15, 17, 18, 21, and 36 as follows.

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Sub B1  
a2 1. (Amended) [Isolated] ~~An isolated~~ [DNA which is the] *ced-3* [gene] nucleic acid, wherein the polypeptide encoded by said nucleic acid is hydrophilic in nature and has a serine rich region, wherein said nucleic acid has the ability to complement *ced-3* or *ced-4* mutations in an *in vivo* or *in vitro* bioassay.

2. (Amended) [Isolated] ~~The isolated~~ [DNA] *ced-3* nucleic acid sequence of claim 1, comprising [having the nucleotide sequence of Figure 4 (Seq ID # 18)] SEQ ID NO: 18.

Sub B2 3. (Amended) [Isolated] ~~The isolated~~ [DNA encoding] *ced-3* nucleic acid sequence of claim 1, comprising a nucleic acid which encodes the amino acid sequence of [Figure 4

A<sup>2</sup> 3  
4. (Amended) [Isolated] An isolated RNA encoded by the [DNA] nucleic acid of claim 1.

B<sup>3</sup>  
A<sup>3</sup>  
8. (Amended) [Isolated] An isolated [DNA] ced-3 nucleic acid sequence, wherein the polypeptide encoded by said nucleic acid is hydrophilic in nature and has a serine rich region, [which is a mutated *ced-3* or *ced-4* gene having a mutation which] comprising a mutation, wherein said mutation affects [the activity of the gene] the ability of said mutated *ced-3* gene to complement *ced-3* or *ced-4* mutations in an *in vivo* or *in vitro* bioassay.

A<sup>4</sup>  
12. (Amended) The [DNA] nucleic acid of claim 8, wherein [the mutated *ced-3* gene] said mutation in *ced-3* is selected from the group consisting of:

- a) n1040;
- b) n718;
- c) n2433;
- d) n1164;
- e) n717;
- f) n1949;

- g) n1286;  
h) n1129;  
i) n1165;  
j) n2430;  
k) n2426; and  
l) n1163

*a*  
of SEQ ID NO:18.

13. (Amended) The [DNA] nucleic acid of claim 8, wherein [the] said mutation in *ced-3* results in an alteration selected from the group consisting of:

- a) a C to T at nucleotide 2310 of SEQ ID NO:18, resulting in a L to F alteration at [codon] position 27 of SEQ ID NO:19;  
b) a G to A at nucleotide 2487 of SEQ ID NO:18, resulting in a G to R alteration at [codon] position 65 of SEQ ID NO:19;  
c) a G to A at nucleotide 5757 of SEQ ID NO:18, resulting in a G to S alteration at [codon] position 360 of SEQ ID NO:19;  
d) a C to T at nucleotide 5940 of SEQ ID NO:18, resulting in a Q to termination alteration at [codon] position 403 of SEQ ID NO: 19;  
e) a C to T at nucleotide 6322 of SEQ ID NO:18, resulting in a Q to termination alteration at [codon] position [417] 412 of SEQ ID NO:19;

f) a G to A at nucleotide 6342 of SEQ ID NO:18, resulting in a W to termination alteration at [codon] position 428 of SEQ ID NO:19;

g) a C to T at nucleotide 6434 of SEQ ID NO:18, resulting in a A to V alteration at [codon] position 449 of SEQ ID NO:19;

a<sup>4</sup>  
h) a C to T at nucleotide 6485, resulting in a A to V alteration at [codon] position 466 of SEQ ID NO:19;

i) a G to A at nucleotide 6535, resulting in a E to K alteration at [codon] position 483 of SEQ ID NO:19;

j) a C to T at nucleotide 7020, resulting in an S to F alteration at [codon] position 486 of SEQ ID NO:19;

k) an alteration in mRNA splicing at nucleotide 6297.

TSB  
14. (Amended) The [DNA] nucleic acid of claim 8, wherein [the] said mutation in *ced-3* is selected from the group consisting of:

a) C to T at nucleotide 2310 of SEQ ID NO: 18;

b) G to A at nucleotide 2487 of SEQ ID NO: 18;

c) G to A at nucleotide 5757 of SEQ ID NO: 18;

d) C to T at nucleotide 5940 of SEQ ID NO: 18;

e) G to A at nucleotide 6297 of SEQ ID NO: 18;

f) C to T at nucleotide 6322 of SEQ ID NO: 18;

g) G to A at nucleotide 6342 of SEQ ID NO: 18;

h) C to T at nucleotide 6434 of SEQ ID NO: 18;

i) C to T at nucleotide 6485 of SEQ ID NO: 18;

j) G to A at nucleotide 6535 of SEQ ID NO: 18;

k) C to T at nucleotide 7020 of SEQ ID NO: 18.

15. (Amended) [Isolated] An isolated RNA encoded by the [DNA] nucleic acid of  
claim 8.

Sub B4  
a5  
17. (Amended) [Isolated] An isolated [DNA] nucleic acid comprising [which is a  
gene selected from the group consisting of]:

(a) a [gene] nucleic acid which is structurally related to the *ced-3* [gene] nucleic acid sequence of SEQ ID NO: 18, wherein the polypeptide encoded by said nucleic acid is hydrophilic in nature and has a serine rich region;

(b) a [gene] nucleic acid which is functionally related to the *ced-3* [gene] nucleic acid, wherein said functionally related nucleic acid encodes a protein that causes cell death, wherein cell death is measured by the ability of said nucleic acid to complement *ced-3* or *ced-4* mutations in an *in vivo* or *in vitro* bioassay; and

(c) a [gene] nucleic acid which is both structurally and functionally related to the *ced-3* [gene] nucleic acid as described in (a) and (b)[;

- By A5 version
- (d) a gene which is structurally related to the *ced-4* gene;
  - (e) a which is functionally related to the *ced-4* gene; and
  - (f) a gene which is both structurally and functionally related to the *ced-4* gene].

18. (Amended) [Isolated] An isolated RNA encoded by the [DNA] nucleic acid of  
claim 17.

A6 B5

21. (Amended) A probe or primer for identifying a gene which is structurally and  
functionally related to the *ced-3* [gene] nucleic acid, which belongs to the same family as  
the *ced-3* nucleic acid, wherein the polypeptide encoded by said nucleic acid sequence is  
hydrophilic in nature and has a serine rich region, wherein said functionally related  
nucleic acid encodes a protein that causes cell death, wherein cell death is measured by  
the ability of said nucleic acid sequence to complement *ced-3* or *ced-4* mutations in an *in*  
*vivo* or *in vitro* bioassay, said probe [which is selected from the group consisting of]  
comprising:

- (a) [DNA] nucleic acid [having] comprising all or a portion of the nucleotide  
sequence of [Figure 4 (Seq. ID # 18)] SEQ ID NO:18;
- (b) RNA encoded by the [DNA] nucleic acid of [a)] SEQ ID NO:18;
- (c) degenerate oligonucleotides derived from a portion of the amino acid sequence  
[of] encoded by the nucleic acid of SEQ ID NO:18 [Figure 4 (Seq. ID.#19); or

(d) an antibody directed against the protein of c)];

(d) nucleic acid comprising the consensus sequence of a conserved region between at least two other genes which belong to the *ced-3* gene family;

(e) degenerate oligonucleotides derived from the consensus sequence of a conserved region between the proteins encoded by at least two other genes which belong to the *ced-3* gene family; or

(f) RNA encoded by d).

36. [The isolated DNA of claim 35, wherein the mutation] An isolated nucleic acid sequence comprising a mutation in the *ced-3* gene, wherein said mutation affects the ability of said mutated *ced-3* gene to complement *ced-3* or *ced-4* mutations in an *in vivo* or *in vitro* bioassay, wherein said mutation [has a result selected from the group consisting of] results from:

- a) inactivation of the [cell death] *ced-3* gene;
- b) constitutive activation of the [cell death] *ced-3* gene; [and] or
- c) production of a mutated *ced-3* gene which does not cause cell death and which antagonizes the activity of functioning cell death genes.

#### Support for the Amendments

The claims have been amended to more precisely define the invention. Support